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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/821,719 | 03/29/2001 | Kathleen A. Donovan | 07039-260001 | 4609 |

26191 7590 08/27/2003

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EXAMINER

HILL, MYRON G

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1648

DATE MAILED: 08/27/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/821,719

Applicant(s)

DONOVAN ET AL.

Examiner

Myron G. Hill

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 17 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4, 5, 8, 15, and 30- 40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4, 5, 8, 15, and 30- 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

This action is in response to Amendment D, filed 12 July 2003.

Claims 4, 5, 8, 15, and 30- 40 are under consideration in this action.

Rejections Withdrawn

Claim Rejections - 35 USC § 112

The rejection of claims 1 and 2 under 35 U.S.C. 112, second paragraph, is withdrawn because the claims were canceled.

The rejection of claims 4,5,8, and 30- 35 under 35 U.S.C. 112, first paragraph, is withdrawn.

Claim Rejections - 35 USC § 103

The rejection of claims 4, 5, 8, and 15 under 35 U.S.C. 103(a) as being unpatentable over Klein (1989 Blood Vol 73, No 2, pages 517- 526) is withdrawn after finding Applicant's argument persuasive that the assay of Klein is not as recited in the claims.

New Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 4, 5, 8, 15, and 30- 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims fail to recite a step of combining the bone marrow preparation with the stromal cells. Furthermore, it is not clear what is meant by "bone marrow preparation". The specification teaches that what is used is a ficoll purified sample of myeloma cells (leaving only MC) and then the supernatant is made cell free and transferred to the culture of stromal cells. The claims fail to accurately recite the details of the assay. Claims 5, 30, 31, and 33- 35 lack proper antecedent basis for the reference to the condition. It is suggested that "in said individual" or phrased as needed be added after MMRPD.

Claims 4, 5, 8, 15, and 30- 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is not clear that the term "monitoring the status" in claims 4, 15, and 32 is supported by the specification in the way it is used in the claims. Applicant is requested to point to specific support for the term. It is suggested that it could be changed to determining if a MMRPD in an individual is likely to progress to active MM which seems to find more clear support in the specification.

Claim Rejections - 35 USC § 103

Claims 4, 5, 8, 15, and 30- 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan and Carter.

The claims are drawn to methods using the steps of assaying for IL-6 in stromal cells for determining if an individual with a MMRPD (multiple myeloma related plasmaproliferative disorder) has a change in IL-6 which measures IL-1beta and indicates a change in disease state or presence of condition when compared to normal.

Donovan teaches that IL-1 beta can differentiate between diagnoses of MM, MGUS, and an unrelated condition (Table 4) and that IL-1 beta and IL-6 have a functional relationship in the cause of and progression to MM (Figure 4 and page 598, column 2- page 599, column 1). Donovan detected full length cDNA that corresponds to expressed mRNA (page 594, column 1, under list of primers). One of ordinary skill in the art would know that there is a direct quantitative correlation between full length mRNA expressed and the protein it makes.

Donovan does not teach stromal cell assay.

Carter teaches a stromal cell co-culture assay using purified myeloma cells (MC) and marrow stromal cells (MSC), that IL-6 is produced in direct proportion to IL-1 beta in the co-culture, and that the production of IL-6 is blocked by anti-IL1 beta antibodies (page 424- 425, Figure 1, and Table 3, also commented on by Donovan, page 599, column 1, top). Thus, one of ordinary skill in the art would know that this MC-MSC assay shows the level of IL-1 beta that is secreted by MC even though the assay reads

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out IL-6 which is produced by the stromal cells in response to the IL-1 produced by the MC.

One of ordinary skill in the art at the time of the invention would have known from the teaching of Donovan that monitoring the status of individuals with MGUS (Table 4) or pre-MM conditions such as SMM (Donovan, Table 1) could have their status monitored or compared to controls because the level of IL1 beta goes from undetectable to detectable. One of ordinary skill in the art at the time of the invention would have known that the level of IL-1 beta could be assayed for with the assay of Carter to determine the status or change of status in an individual diagnosed with MGUS or related pre-MM condition. One of ordinary skill in the art would know that because the IL-1 is secreted, that a cell free supernatant of the MC can be assayed for the presence of IL-1 as well.

Thus, it would have been *prima facie* obvious to determine the status of an individual using the criteria of Donovan with the assay of Carter to determine the IL-1 beta that leads to IL-6 production in a stromal cell assay.

Conclusion

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4247. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Myron G. Hill
Patent Examiner
15 August 2003



JAMES HOUSEL 8/14/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600